

## Review Article

# A Review of the Antimicrobial Potential of *Musca domestica* as a Natural Approach with Promising Prospects to Countermeasure Antibiotic Resistance

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Drug-resistant pathogens have become a serious public health concern worldwide considering the rapid emergence and distribution of new strains, which outpace the development of antimicrobial drugs. It is a complex and serious clinical problem that can cause an epidemic of a disease; consequently, numerous research studies are conducted to determine the solution to these problems, including the development of new antibiotics derived from natural sources such as insects. The housefly (*Musca domestica* L.), an insect known as a cosmopolitan pest, possesses several qualities that can ameliorate diseases; consequently, they can be used as a bioactive component in the development of medicines. These qualities include its potential as a source of antibacterial agents. The external surface components, wings, internal organs, and whole body extract of *M. domestica* can all contribute antimicrobial potential due to bioactive compounds they produce. This article discusses several antimicrobial properties of *M. domestica* that could be utilized for healthcare benefits.

## 1. Introduction

Drug-resistant pathogens present an ever-increasing global health threat due to the rapid emergence and distribution of new strains which is faster than the development of antimicrobial drugs [1–3]. This circumstance may result in the inappropriate or excessive utilization of antibiotics [4, 5]. There have been cases recorded of multidrug-resistant bacterial infection caused by *Escherichia coli* [6], methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus pneumoniae*, vancomycin-resistant *Enterococcus* (VRE), *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Mycobacterium tuberculosis*. These antimicrobial-resistant superbugs have caused an alarming death rate of

over 50% in certain regions [7]. It is a complex and serious clinical problem that can cause an epidemic of a disease, and hence several research studies are conducted to establish the solution to these problems, including the development of new antibiotics derived from nature, such as insects [6, 8, 9].

Insects and arthropods are considered a vast, unexplored, and underutilized source of potentially useful compounds for contemporary modern medicine [10]. They have a long history as a traditional therapy for humans and now have become more popular and are being developed for use in evidence-based practice [11, 12], in addition to becoming an important alternative therapy in the modern age in several countries such as India, Mexico, Korea, China, Spain, Brazil, Argentina, Ecuador, and several African countries [10, 13].

The housefly (*Musca domestica* L.) is among the Dipteran group and is a well-known cosmopolitan pest of livestock, poultry, and human dwellings. Houseflies are typically associated with humans or human activity [14]. Female houseflies lay countless eggs in animal waste, garbage, and other decaying matter [15]. The insect undergoes a complete life cycle, consisting of egg, larval, pupal, and adult stages, in 7 to 10 days [14]. They will live for 60 days the longest [15]. They prefer warm weather for optimal development, and hence they may thrive in the summer [16].

*M. domestica* is a vector for disease-causing bacteria due to its hopping and feeding behavior on a variety of pathogen-infested substrates [17, 18]. They also contribute to the spread of antibiotic-resistant bacteria, which can raise public health concerns [19]. However, contrary to the adult's existence as a vector for several diseases, the larvae of *M. domestica* has been used in the treatment of infectious diseases in Latin America and several other treatments for osteomyelitis, decubitus ulcers, eczema, malnutrition, and gastric cancer in China since the Qing and Ming dynasties until present days [6, 10, 13]. Due to the fact that scientific evidence has demonstrated that *M. domestica* larvae possess a variety of properties that can ameliorate diseases, they can be used as a source of bioactive component for pharmaceutical development [15, 20, 21]. These qualities include potential as antibacterial agents [10], even against bacteria that have developed multidrug resistance [6].

Housefly antimicrobial potential can come from the external surface components [15, 20, 22] and internal organs such as the digestive tract [6], hemolymph [23], and the insect's whole body extract [24, 25]. Therefore, this article focuses on the antimicrobial potentials that can be isolated from *M. domestica* and utilized for therapeutic purposes.

## 2. Microorganisms Contained in the Body Parts of *M. domestica*

Houseflies have a close association with microorganisms and their environments, especially at a crucial moment in each developmental stage [26]. The internal bacterial community of houseflies from various locations is similar and relatively stable, whereas the external bacterial community is affected by geography and habitat [27]. Several specific microbiota species isolated from various body parts of *M. domestica* are depicted in Table 1.

Bahrndorff et al. [28] reported that Firmicutes, Actinobacteria, Proteobacteria, and Bacteroidetes are phyla that dominate the entire microbiota of houseflies from 10 dairy farms in Denmark. In addition, Laziz et al. [22] isolated and identified 300 samples of houseflies (*M. domestica*) collected from different areas in Kirkuk City (Iraq) and found several species of Gram-positive and Gram-negative bacteria associated with body surface on the head, thorax, and abdomen (45.2%), right wing (35.7%), and left wing (19.1%). de Jonge et al. [29] revealed that *M. domestica*, both female and male, have a different population of bacteria in every segment of their digestive tracks.

The crop segment is abundant with *Streptococcus*, *Lactococcus*, *Leuconostoc*, and *Chishuiella*; the midgut segment is rich with *Delftia*, *Chryseobacterium*, *Acidovorax*, *Comamonas*,

*Spirosoma*, and *Sphingomonas*; meanwhile other bacterial colonies found in both segments are *Pelagibacterium*, *Fructobacillus*, *Lactobacillus*, *Dyadobacter*, and *Novosphingobium*. The following bacterial phyla are present in accordance with the life cycle of the housefly: Firmicutes are abundant during the larval stages and are considered early colonizers, but as they mature into adults, Proteobacteria and Bacteroidetes take over. On the other hand, bacteria that exist throughout all stages are *Lactococcus*, *Lactobacillus*, and *Enterococcus*, while *Weissella* and *Chishuiella* were found in newly hatched larvae and adults, respectively.

Kanan et al. [30] successfully identified seven bacteria from houseflies sampled from Luwuk, Central Sulawesi, Indonesia, which previously had never been reported to be associated with flies. Nazari et al. [19] discovered that bacteria from the highest to lowest prevalence, respectively, are *Bacillus* spp. followed by *Staphylococcus* spp., *E. coli*, and *Enterococcus* spp. Yalli et al. [31] isolated *E. coli*, *Pseudomonas* spp., *Bacillus* spp., *Enterobacter* spp., *Staphylococcus* spp., *Salmonella* spp., *Proteus* spp., and *Klebsiella* spp. on the body surface of houseflies obtained from the kitchen, toilet, and room in Sokoto (Nigeria). Moreover, Nazni et al. [32] found *Bacillus* sp., *Coccobacillus* sp., *Staphylococcus* sp., *Micrococcus* sp., *Streptococcus* sp., *Acinetobacter* sp., *Enterobacter* sp., *Proteus* sp., *Klebsiella* sp., and yeast cell isolated from feces, vomitus, external surfaces, and internal organs of housefly collected from several regions in Malaysia.

## 3. Antimicrobial Potentials of *M. domestica*

Secondary metabolites account for the majority of antimicrobials produced by microorganisms [9]. Insect physiology, such as resistance to pathogenic organisms, is influenced by numerous factors, including the gut microorganisms within the insect body [28]. *M. domestica* is known to have a diverse microbiome with antagonistic or antimicrobial properties that can impede the growth of pathogenic bacteria originating from the previous substrate [33]. Antagonistic activities from these bacteria may be associated with their abilities to secrete enzymes or compounds that function antagonistically and/or as an antimicrobial [18]. Table 2 and Figure 1 show various antimicrobial components belonging to *M. domestica*, which are derived from various parts of their body, and the bacteria that are the targets of these antimicrobials.

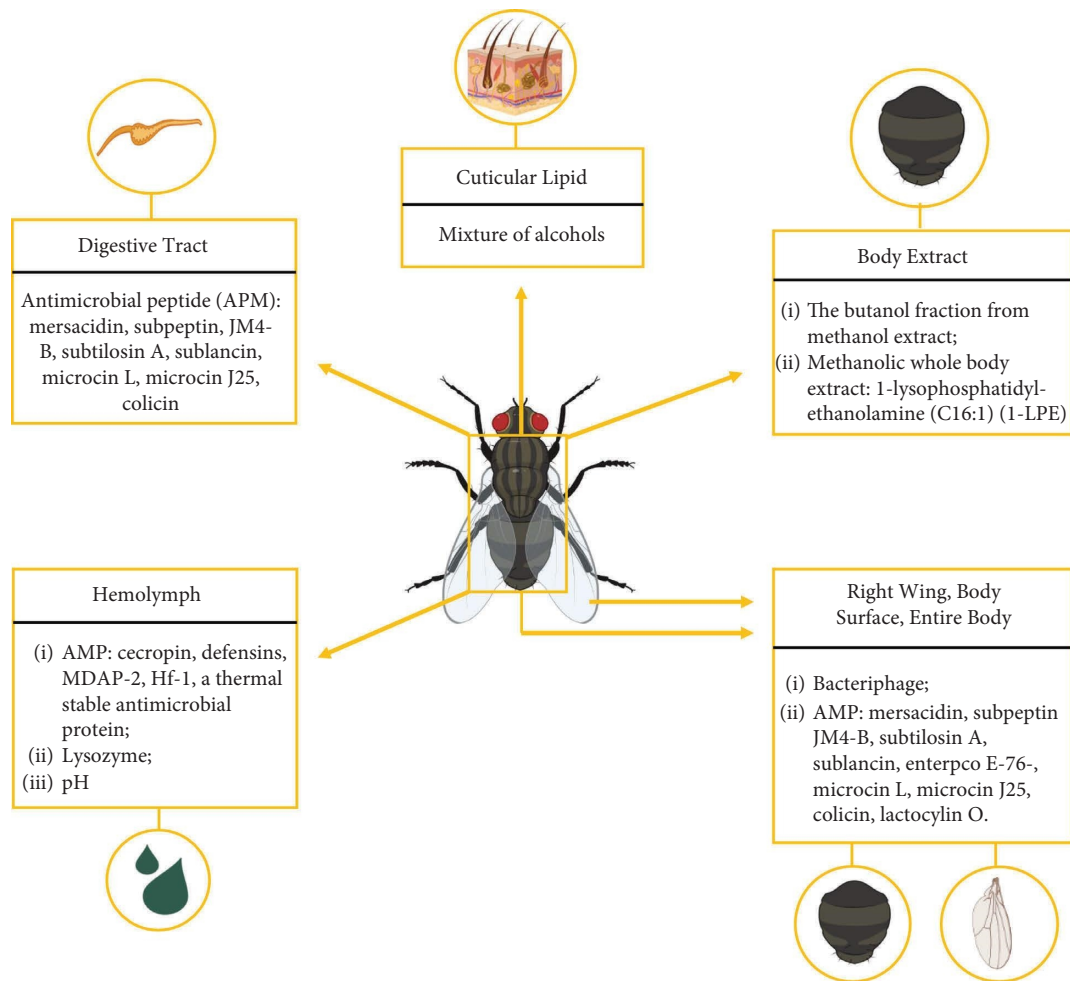
The production of early antimicrobial compounds by *M. domestica* larvae may protect the housefly from pathogenic microbes during the next developmental stages until it becomes an adult. These early antimicrobial compounds could be the primary antimicrobial compounds in their defense [43–45]. The presence of bacteria in the digestive system of a housefly indicates that *M. domestica* digestive tract produces antimicrobial compounds. These antimicrobial-producing bacteria in the wings and guts of insects are linked to their feeding behavior on microbe-contaminated substrates and stimulate the resistance response [18]. Laziz et al. [22] discovered that *B. subtilis* isolated from the right wing and body surface of *M. domestica* effectively inhibited the growth of *Pseudomonas* spp. *B. subtilis* plays an important role in the

TABLE 1: The type of bacteria isolated from housefly *M. domestica*.

Body part	Isolated microorganisms	References
Entire body	(i) Actinobacteria ( <i>Microbacterium</i> spp.)	Bahrdorff et al. [28] de Jonge et al. [29]
	(ii) Bacteroidetes/Bacteroidota ( <i>Apibacter</i> spp., <i>Chishuiella</i> spp., <i>Chryseobacterium</i> spp., <i>Moheibacter</i> spp., <i>Spirosoma</i> spp., <i>Sphingobacterium</i> spp.)	
	(iii) Firmicutes ( <i>Bacillus</i> spp., <i>Enterococcus</i> spp., <i>Lactobacillus</i> spp., <i>Lactococcus</i> spp., <i>Leuconostoc</i> spp., <i>Weissella</i> spp.)	
	(iv) Fusobacteria	
	(v) Lentisphaerota/Lentisphaerae	
	(vi) Proteobacteria ( <i>Acidovorax</i> spp., <i>Alcaligenes</i> spp., <i>Brevundimonas</i> spp., <i>Delftia</i> spp., <i>Klebsiella</i> spp., <i>Ochrobactrum</i> spp., <i>Paenochrobactrum</i> spp., <i>Pseudochrobactrum</i> spp., <i>Pseudomonas</i> spp., <i>Stenotrophomonas</i> spp.)	
	(vii) Saccharibacteria (formerly known as TM7)	
	(viii) Spirochaetota/Spirochaetes	
	(ix) Tenericutes	
Right wing	(i) Actinobacteria ( <i>Micrococcus luteus</i> )	Laziz et al. [22] Kanan et al. [30]
	(ii) Bacteroidetes/Bacteroidota ( <i>Sphingobacterium</i> sp.)	
	(iii) Firmicutes ( <i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>S. xylosus</i> )	
	(iv) Proteobacteria ( <i>Acinetobacter</i> spp., <i>Brucella melitensis</i> , <i>Escherichia coli</i> , <i>Klebsiella oxytoca</i> , <i>Proteus vulgaris</i> , <i>P. fluorescens</i> )	
Left wing	(i) Actinobacteria ( <i>Bifidobacterium minimum</i> )	Laziz et al. [22] Kanan et al. 2020 [30]
	(ii) Bacteroidetes/Bacteroidota ( <i>Sphingobacterium</i> sp.)	
	(iii) Firmicutes ( <i>Bacillus</i> spp., <i>Aerococcus viridans</i> , <i>Streptococcus iniae</i> )	
	(iv) Proteobacteria ( <i>Acinetobacter</i> spp., <i>Alcaligenes faecalis</i> , <i>Brucella melitensis</i> bv.1, <i>Enterobacter asburiae</i> , <i>P. fluorescens</i> )	
Body surfaces	(i) Firmicutes ( <i>Bacillus cereus</i> , Coagulase-negative <i>Staphylococcus</i> , <i>Enterococcus</i> spp., <i>S. aureus</i> , <i>S. saprophyticus</i> )	Laziz et al. [22] Nazari et al. [19] Yalli et al. [31]
	(ii) Proteobacteria ( <i>E. coli</i> , <i>Citrobacter</i> spp., <i>Enterobacter</i> spp., <i>Haemophilus ducreyi</i> , <i>Hafnia alvei</i> , <i>Klebsiella</i> spp., <i>K. oxytoca</i> , <i>Proteus</i> spp., <i>P. aeruginosa</i> , <i>Pseudomonas</i> spp., <i>Serratia fonticola</i> )	
Digestive tract	(i) Firmicutes ( <i>Bacillus</i> sp.)	Nazni et al. [32]
	(ii) Proteobacteria ( <i>Enterobacter</i> spp., <i>E. coli</i> , <i>Klebsiella</i> spp., <i>Proteus</i> spp.)	

TABLE 2: Antimicrobial components of *M. domestica* microbiome.

Body parts	Microbiome metabolites	Inhibited bacteria	References
Right wing, body surface, entire body	(i) Bacteriophage	(i) <i>Pseudomonas</i> spp.	(i) Laziz et al. [22]
	(ii) Antimicrobial peptide (AMP): mersacidin, subpeptin JM4-B, subtilisin A, sublancin, enterpco E-760, microcin L, microcin J25, colicin, lactocyclacin Q	(ii) <i>E. coli</i> (iii) MRSA, <i>Streptococcus pyogenes</i> , <i>S. agalactiae</i> , and <i>S. pneumoniae</i> (iv) <i>S. aureus</i> , <i>S. faecalis</i> , <i>Salmonella</i> sp., and <i>Shigella flexneri</i> (v) <i>Enterococcus faecalis</i> and <i>Listeria monocytogenes</i> (vi) <i>Yersinia</i> spp., <i>Campylobacter</i> spp. <i>Staphylococcus</i> spp. <i>Listeria monocytogenes</i> (vii) <i>Pseudomonas aeruginosa</i> (viii) <i>Lactococcus</i> spp.	(ii) Claresta et al. [20]; Zhao et al. [34] (iii) Simons et al. [35] (iv) Yang et al. [36]
	(i) AMP: cecropin, defensins, Hf-1, MDAP-2, a thermal stable antimicrobial protein (ii) Lysozyme	<i>S. aureus</i> , <i>S. epidermidis</i> , and <i>P. aeruginosa</i>	(i) Liang et al. [37]; Wang et al. [38]; Dang et al. [39]; Hou et al. [10]; Pei et al. [40]; Hao et al. [41] (ii) Kawasaki and Andoh [42]
	(i) The butanol fraction obtained from ethanol (ii) Methanolic whole body extract: 1-lysophosphatidylethanolamine (C <sub>16:1</sub> ) (1-LPE)	(i) MRSA and VRE strains (ii) <i>B. thuringiensis</i> and <i>Saccharomyces cerevisiae</i>	(i) Park et al. [25] (ii) Meylaers [24]
Cuticular lipid	Mixtures of alcohols	<i>Rhodococcus equi</i> , <i>Candida lipolytica</i> , <i>C. tropicalis</i>	(i) Gołebiowski [14]
Digestive track	AMP: mersacidin, subpeptin JM4-B, subtilisin A, sublancin, microcin L, microcin J25, and colicin	(i) MRSA, <i>Streptococcus pyogenes</i> , <i>S. agalactiae</i> , and <i>S. pneumoniae</i> (ii) <i>S. aureus</i> , <i>S. faecalis</i> , <i>Salmonella</i> sp., and <i>Shigella flexneri</i> (iii) <i>Enterococcus faecalis</i> and <i>Listeria monocytogenes</i> (iv) <i>E. coli</i> , <i>Salmonella enterica</i> , <i>Shigella</i> spp., and <i>Pseudomonas aeruginosa</i>	(i) Simons et al. [35] (ii) Yang et al. [36]

FIGURE 1: Antimicrobial components of *M. domestica* and their sources.

production of antibiotics, enzymes, and other secondary metabolites that possess a broad spectrum of antimicrobial activities against pathogenic microbes [46]. The right wing of *M. domestica* contains *B. subtilis* and *B. circulans* that can neutralize *E. coli* contaminated drinks due to their antibiotic effects. The enzymes and other secondary metabolites they produce can inhibit activities of several pathogenic microbes such as bacteria, fungi/yeasts, and parasites [20, 34]. Furthermore, the right wing contains bacteriophage, which is thought to produce endolysins (phage lysins), which causes bacterial cell lysis [20].

Another component of *M. domestica* that acts as a defense against microbes is hemolymph. This bactericidal effect from the hemolymph may counter-attack several bacteria including *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Pseudomonas aeruginosa* [42]. Hemolymph is a clear fluid (with or without greenish-yellow pigmentation) that contains very complex chemicals, mostly consisting of immune proteins and carbohydrates such as antimicrobial peptides (AMP), lysozyme, and agglutinins [23, 40, 47]. AMP is an innate immunity effector against bacteria, fungi, parasites, and viruses that possess several common properties such as cationicity, hydrophobicity, and amphipathicity for their antimicrobial activities [33]. A

number of AMPs found in houseflies are cecropin [37], defensins [39, 48], MDAP-2 [40], and Hf-1 [10], as well as a cationic antimicrobial protein with a molecular weight of 16,315 D that is thermally stable and resistant to freezing and thawing [41]. AMPs are synthesized by immune and epithelial cells and secreted into hemolymph in response to infection and the presence of pathogenic bacteria [18]. The mechanisms of AMPs include binding to DNA, RNA, or intracellular protein [9] as well as inhibition of membrane protein and cell wall synthesis, altering the permeability of target cells [41]. Additionally, AMPs also induce apoptosis in eukaryotic cells and autolysis in bacterial cells and inhibit enzymes produced by some microbes, thereby reducing their virulence [9].

Another vital AMP is bacteriocin [35, 36]. *Bacillus* spp. found in the wings, digestives tract, and entire body of *M. domestica* produces bacteriocins such as mersacidin, subpeptin JM4-B, subtilisin A, and sublancin [35]. On the other hand, *Enterococcus* sp., which is found in the entire body and body surface, produces enterpco E-760 [35]. *Lactococcus* spp., which is found throughout the body, produces the lactic clinic Q. Body surfaces, the right wing, and the digestive tract harbor *E. coli* that produce microcin L, microcin J25, and colicin [35, 36].

The peritrophic matrix/membrane (PM protein) in a housefly's midgut plays a crucial role in preventing infection from outside microbes. The novel PM protein, MdPM-17, has been isolated from the housefly larvae. Several essential components of AMPs, including defensins, cecropins, and dipterin, are expressed by MdPM-17 recombinant protein silencing via RNA interference. This mechanism encourages the association between the MdPM-17 protein and the antibacterial response of houseflies [38]. Lysozymes are considered one of the innate immune effectors in flies that function in degrading pathogenic microbes [49]. As an antibacterial enzyme, lysozyme cleaves the  $\beta$ -1.4 glycosidic bond between N-acetylmuramic acid and N-acetylglucosamine, which are major components of the peptidoglycan structure of a bacterial cell wall [18]. Lysozyme activity is affected by several factors, including enzyme activity, pH level, and some effectors such as AMPs, which function to combat bacterial infections when the number is at an alarming level [44]. Lysozyme exerts its complex antibacterial defense strategies in response to infections [23]. Besides antibacterial proteins and carbohydrates in the hemolymph, it is possible that bactericidal potential is related to the acidity level (pH) through the increase of bacterial activities because of the decrease in pH level.

Additionally, other antimicrobial potentials of housefly can be seen from the butanol fraction obtained from ethanol extract of its larvae which demonstrate antibacterial activity against the methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE strains) [25]. Housefly is also efficiently protected from infection by common pathogens inhabiting similar habitats through the association between the innate immunity mechanisms with mixtures of alcohols found in cuticular lipids of all stages (larvae, pupae, and adults) [14]. Moreover, 1-lysophosphatidylethanolamine ( $C_{16:1}$ ) (1-LPE) which is extracted from healthy uninfected last instar larvae can interfere with the growth of the Gram-positive bacteria (*Bacillus thuringiensis*) and the yeast *Saccharomyces cerevisiae* [24].

#### 4. Conclusion

Evidence from a number of studies indicates that the common house fly, *Musca domestica*, possesses bioactive compounds with antimicrobial potential. These compounds originate from its organ components and the diverse microbiomes it harbors. The antagonistic activities of the diverse microbiome isolated from insect body parts are thought to be related to the ability to secrete enzymes or compounds that function as antimicrobial. Bacteriophage, AMP, lysozyme, pH, and alcohols contained in this insect have a direct or indirect bactericidal effect. However, a substantial amount of research is still required to investigate and develop the antimicrobial potentials of houseflies.

#### Abbreviations

AMPs: Antimicrobial peptides  
LPE: Lysophosphatidylethanolamine  
MRSA: Methicillin-resistant *Staphylococcus aureus*

PM: Peritrophic matrix/membrane  
VRE: Vancomycin-resistant *Enterococcus*.

#### Data Availability

The research data are presented in the article. These data are publicly available and accessible online. Detailed sources are provided in References of the article.

#### Conflicts of Interest

The authors declare that they have no conflicts of interest.

#### Authors' Contributions

Nurdjannah Jane Niode was responsible for conceptualisation, investigation, formal analysis, original draft preparation, and review and editing. Trina Ekawati Tallei was responsible for conceptualisation, investigation, formal analysis, and review and editing. Billy Johnson Kepel was responsible for conceptualisation, investigation, and formal analysis. Charles Kurnia Mahono was responsible for investigation, validation, and review and editing. Felicia Maria Lolong was responsible for investigation, validation, and original draft preparation. Merina Pingkan Matheos was responsible for validation and original draft preparation.

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#### References

- [1] H. Jamali, M. Paydar, B. Radmehr, S. Ismail, and A. Dadrasnia, "Prevalence and antimicrobial resistance of *Staphylococcus aureus* isolated from raw milk and dairy products," *Food Control*, vol. 54, pp. 383–388, 2015.
- [2] D. A. Dargatz, C. A. Koprak, M. M. Erdman, and P. J. Fedorka-Cray, "Prevalence and antimicrobial resistance of salmonella isolated from cattle feces in United States Feedlots in 2011," *Foodborne Pathogens and Disease*, vol. 13, no. 9, pp. 483–489, 2016.
- [3] K. S. Kaye and J. M. Pogue, "Infections caused by resistant gram-negative bacteria: epidemiology and management," *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, vol. 35, no. 10, pp. 949–962, 2015.
- [4] G. Guo, R. Tao, Y. Li et al., "Identification and characterization of a novel antimicrobial protein from the housefly *Musca domestica*," *Biochemical and Biophysical Research Communications*, vol. 490, no. 3, pp. 746–752, 2017.
- [5] WHO, "Antimicrobial resistance," 2021, <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>.
- [6] X. Lu, J. Shen, X. Jin et al., "Bactericidal activity of *Musca domestica* cecropin (Mdc) on multidrug-resistant clinical isolate of *Escherichia coli*," *Applied Microbiology and Biotechnology*, vol. 95, no. 4, pp. 939–945, 2012.
- [7] L. Alkema, V. Kantorova, C. Menozzi, and A. Biddlecom, "National, regional, and global rates and trends in

- contraceptive prevalence and unmet need for family planning between 1990 and 2015: a systematic and comprehensive analysis," *The Lancet*, vol. 381, no. 9878, pp. 1642–1652, 2013.
- [8] N. J. Niode, A. Adji, J. Rimbing et al., "In silico and in vitro evaluation of the antimicrobial potential of *Bacillus cereus* isolated from *Apis dorsata* gut against *Neisseria gonorrhoeae*," *Antibiotics*, vol. 10, no. 11, pp. 1401–1421, 2021.
  - [9] S. M. Ali, R. Siddiqui, and N. A. Khan, "Antimicrobial discovery from natural and unusual sources," *Journal of Pharmacy and Pharmacology*, vol. 70, no. 10, pp. 1287–1300, 2018.
  - [10] L. Hou, Y. Shi, P. Zhai, and G. Le, "Antibacterial activity and in vitro anti-tumor activity of the extract of the larvae of the housefly (*Musca domestica*)," *Journal of Ethnopharmacology*, vol. 111, no. 2, pp. 227–231, 2007.
  - [11] N. Ratcliffe, P. Azambuja, and C. B. Mello, "Recent advances in developing insect natural products as potential modern day medicines," *Evidence-based Complementary and Alternative Medicine*, vol. 201421 pages, 2014.
  - [12] E. P. Cherniack, "Bugs as drugs, Part 1: insects. The new alternative medicine for the 21st century," *Alternative Medicine Review: A Journal of Clinical Therapeutic*, vol. 15, no. 2, pp. 124–135, 2010.
  - [13] L. Seabrooks and L. Hu, "Insects: an underrepresented resource for the discovery of biologically active natural products," *Acta Pharmaceutica Sinica B*, vol. 7, no. 4, pp. 409–426, 2017.
  - [14] M. Gołębowski, M. Dawgul, W. Kamysz et al., "The antimicrobial activity of the alcohols from *Musca domestica*," *Journal of Experimental Biology*, vol. 215, no. 19, pp. 3419–3428, 2012.
  - [15] R. M. Atta, "Microbiological studies on fly wings (*Musca domestica*) where disease and treat," *World Journal of Medical Sciences*, vol. 11, no. 4, pp. 486–489, 2014.
  - [16] T. A. Dellinger and E. Day, "House fly *Musca domestica* L. Diptera: muscidae," 2021, [https://www.pubs.ext.vt.edu/content/dam/pubs\\_ext\\_vt\\_edu/ENTO/ENTO-137/ENTO-137-pdf.pdf](https://www.pubs.ext.vt.edu/content/dam/pubs_ext_vt_edu/ENTO/ENTO-137/ENTO-137-pdf.pdf).
  - [17] M. C. Monyama, E. T. Onyiche, M. O. Taioe, J. S. Nkhebenyane, and O. M. M. Thekisoe, *Bacterial Pathogens Identified From Houseflies in Different Human and Animal Settings: A Systematic Review and Meta-Analysis*, Wiley, Hoboken, NJ, USA, pp. 1–18, 2021.
  - [18] M. Asril, I. A. Rini, I. Oktaviani, and M. Mushaliyah, "Tracking the source of antimicrobial production from house fly (*Musca domestica*): right-wing of fly or gut system? - a mini-review," *Elkawanie*, vol. 7, no. 2, pp. 225–238, 2022.
  - [19] M. Nazari, T. Mehrabi, S. M. Hosseini, and M. Y. Alikhani, "Bacterial contamination of adult house flies (*Musca domestica*) and sensitivity of these bacteria to various antibiotics, captured from hamadan city, Iran," *Journal of Clinical and Diagnostic Research: Journal of Clinical and Diagnostic Research*, vol. 11, no. 4, pp. DC04–7, 2017.
  - [20] I. Claresta, D. D. Sari, S. Nurohmi, Y. A. Damayanti, and A. Y. Damayanti, "The right-wing of fly (*Musca domestica*) as a neutralization of drinks contaminated by microbe," *Journal of Nutritional Science and Vitaminology*, vol. 66, pp. S283–S285, 2020.
  - [21] N. A. Baeshen, N. T. Elsharawy, N. N. Baeshen, and M. N. Baeshen, "The effect of natural falling and dipping of house fly (*Musca domestica*) on the microbial contamination of water and milk," *Journal of Food: Microbiology, Safety & Hygiene*, vol. 7, no. 3, pp. 1–4, 2022.
  - [22] F. W. A. Laziz, B. M. Muhammed, and H. Alishareef, "Antagonistic activity between bacterial species carried by adult house fly *Musca domestica*," *Journal of Cardiovascular Disease Research*, vol. 12, no. 3, pp. 2961–2968, 2021.
  - [23] A. Z. Sahalan, B. Omar, A. Y. Mohamed, and J. Jeffery, "Antibacterial activity of extracted hemolymph from larvae and pupae of local fly species, *Musca domestica* and *Chrysomya megacephala*," *Jurnal Sains Kesihatan Malaysia*, vol. 4, no. 2, pp. 1–11, 2007.
  - [24] K. Meylaers, E. Clynen, D. Daloze, A. DeLoof, and L. Schoofs, "Identification of 1-lysophosphatidylethanolamine (C16:1) as an antimicrobial compound in the housefly, *Musca domestica*," *Insect Biochemistry and Molecular Biology*, vol. 34, no. 1, pp. 43–49, 2004.
  - [25] S. O. Park, J. H. Shin, W. K. Choi, B. S. Park, J. S. Oh, and A. Jang, "Antibacterial activity of house fly-maggot extracts against MRSA (Methicillin-Resistant *Staphylococcus aureus*) and VRE (Vancomycin-Resistant enterococci)," *Journal of Environmental Biology*, vol. 31, no. 5, pp. 865–871, 2010.
  - [26] D. Nayduch and R. G. Burrus, "Flourishing in filth: house fly-microbe interactions across life history," *Annals of the Entomological Society of America*, vol. 110, no. 1, pp. 6–18, 2017.
  - [27] R. Park, M. C. Dzialo, S. Spaepen et al., "Microbial communities of the house fly *Musca domestica* vary with geographical location and habitat," *Microbiome*, vol. 7, pp. 147–212, 2019.
  - [28] S. Bahrndorff, N. de Jonge, H. Skovgård, and J. L. Nielsen, "Bacterial communities associated with houseflies (*Musca domestica* L.) sampled within and between farms," *PLoS One*, vol. 12, no. 1, 2017.
  - [29] N. de Jonge, T. Y. Michaelsen, R. Ejbye-Ernst et al., "Housefly (*Musca domestica* L.) associated microbiota across different life stages," *Scientific Reports*, vol. 10, pp. 7842–7849, 2020.
  - [30] M. Kanan, C. Salaki, and Y. S. Mokosuli, "Molecular identification of bacterial species from *Musca domestica* L. And *Chrysomya megacephala* L. In Luwuk city, central Sulawesi, Indonesia," *Journal of Pure and Applied Microbiology*, vol. 14, no. 2, pp. 1595–1607, 2020.
  - [31] A. A. Yalli, S. Sambo, H. M. Lawal, and U. Tukur, "Study of bacteria on the body surfaces of house flies (*Musca domestica*) in some homes within Sokoto metropolis," *Journal of Advancement in Medical and Life Sciences*, vol. 5, no. 4, pp. 1–5, 2017.
  - [32] W. A. Nazni, B. Seleena, H. L. Lee, J. Jeffery, T. A. R. T. Rogayah, and M. A. Sofian, "Bacteria fauna from the house fly, *Musca domestica* (L.)," *Tropical Biomedicine*, vol. 22, no. 2, pp. 225–231, 2005.
  - [33] S. Qi, B. Gao, and S. Zhu, "Molecular diversity and evolution of antimicrobial peptides in *Musca domestica*," *Diversity*, vol. 13, no. 3, pp. 107–129, 2021.
  - [34] Y. Zhao, W. Wang, F. Zhu, X. Wang, X. Wang, and C. Lei, "The gut microbiota in larvae of the housefly *Musca domestica* and their horizontal transfer through feeding," *AMB Express*, vol. 7, no. 1, pp. 147–149, 2017.
  - [35] A. Simons, K. Alhanout, and R. E. Duval, *Bacteriocins, antimicrobial peptides from bacterial origin: Overview of their biology and their impact against multidrug-resistant bacteria*, Microorganisms. MDPI AG, vol. 8, Basel, Switzerland, , 2020.
  - [36] S. C. Yang, C. H. Lin, C. T. Sung, and J. Y. Fang, "Antibacterial activities of bacteriocins: application in foods and pharmaceuticals," *Frontiers in Microbiology*, vol. 5, 2014.
  - [37] Y. Liang, J. X. Wang, X. F. Zhao, X. J. Du, and J. F. Xue, "Molecular cloning and characterization of cecropin from the housefly (*Musca domestica*), and its expression in *Escherichia coli*," *Developmental & Comparative Immunology*, vol. 30, no. 3, pp. 249–257, 2006.

- [38] Y. Wang, J. Cheng, M. Luo, J. Wu, and G. Guo, "Identifying and characterizing a novel peritrophic matrix protein (MdPM-17) associated with antibacterial response from the housefly, *Musca domestica* (Diptera: muscidae)," *Journal of Insect Science*, vol. 20, no. 6, pp. 34–37, 2020.
- [39] X. L. Dang, Y. S. Wang, Y. D. Huang, X. Q. Yu, and W. Q. Zhang, "Purification and characterization of an antimicrobial peptide, insect defensin, from immunized house fly (Diptera: muscidae)," *Journal of Medical Entomology*, vol. 47, no. 6, pp. 1141–1145, 2010.
- [40] Z. Pei, X. Sun, Y. Tang, K. Wang, Y. Gao, and H. Ma, "Cloning, expression, and purification of A new antimicrobial peptide gene from *Musca domestica* larva," *Gene*, vol. 549, no. 1, pp. 41–45, 2014.
- [41] Y. J. Hao, Y. J. Jing, H. Qu, D. S. Li, and R. Q. Du, "Purification and characterization of A thermal stable antimicrobial protein from housefly larvae, *Musca domestica*, induced by ultrasonic wave," *Acta Biologica Hungarica*, vol. 59, no. 3, pp. 289–304, 2008.
- [42] K. Kawasaki and M. Andoh, "Properties of induced antimicrobial activity in *Musca domestica* larvae," *Drug Discoveries & Therapeutics*, vol. 11, no. 3, pp. 156–160, 2017.
- [43] M. Petridis, M. Bagdasarian, M. K. Waldor, and E. Walker, "Horizontal transfer of shiga toxin and antibiotic resistance genes among *Escherichia coli* strains in house fly (Diptera: muscidae) gut," *Journal of Medical Entomology*, vol. 43, no. 2, pp. 288–295, 2006.
- [44] D. Nayduch and C. Joyner, "Expression of lysozyme in the life history of the house fly (*Musca domestica* L.)," *Journal of Medical Entomology*, vol. 50, no. 4, pp. 847–852, 2013.
- [45] M. Akhtar, H. Hirt, and L. Zurek, "Horizontal transfer of the tetracycline resistance gene tetm mediated by Pcf10 among *Enterococcus faecalis* in the house fly (*Musca domestica* L.) alimentary canal," *Microbial Ecology*, vol. 58, no. 3, pp. 509–518, 2009.
- [46] Y. Su, C. Liu, H. Fang, and D. Zhang, "Bacillus subtilis: a universal cell factory for industry, agriculture, biomaterials and medicine," *Microbial Cell Factories*, vol. 19, no. 1, pp. 173–212, 2020.
- [47] I. El-Garawani, H. El-Seedi, S. Khalifa, I. H. el Azab, M. Abouhendia, and S. Mahmoud, "Enhanced antioxidant and cytotoxic potentials of lipopolysaccharides-injected musca domestica larvae," *Pharmaceutics*, vol. 12, no. 11, pp. 1111–1115, 2020.
- [48] J. X. Wang, X. F. Zhao, Y. L. Liang et al., "Molecular characterization and expression of the antimicrobial peptide defensin from the housefly (*Musca domestica*)," *Cellular and Molecular Life Sciences*, vol. 63, no. 24, pp. 3072–3082, 2006.
- [49] C. Gill, S. Bahrndorff, and C. Lowenberger, "Campylobacter jejuni in *Musca domestica*: an examination of survival and transmission potential in light of the innate immune responses of the house flies," *Insect Science*, vol. 24, no. 4, pp. 584–598, 2017.